

# Boronolide: Structure and Stereochemistry (X-Ray Analysis)

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**Boronolide, a naturally occurring  $\alpha,\beta$ -unsaturated C<sub>12</sub>-lactone containing four asymmetric centres, three of which are of unknown chirality, has been subjected to a crystal structure determination on the basis of single crystal X-ray diffraction data collected at 120 K. The final *R*-value for 862 reflections and 145 parameters became 0.043. The X-ray analysis established the chemical structure of boronolide as 6*R*-(1*R*,2*R*,3*S*)-5,6-dihydro-6-[1,2,3-tris(acetyloxy)-heptyl]-2*H*-pyran-2-one.**

Several years ago, a crystalline,  $\alpha,\beta$ -unsaturated lactone, boronolide, was isolated in one of the authors' (J.P.) laboratory from stems and bark of *Tetradenia fruticosa* Benth., an endemic Madagascan member of the family Labiatae, recognized and valued in local folk medicine under the names 'Borona' or 'Borondahy'. The structure *1* was proposed for boronolide, based on spectroscopical data, chemical degradation, and chiroptical analyses, yet without specification of stereochemistry at the three exocyclic chiral centres.<sup>1</sup>

In connection with other studies, the detailed stereochemistry of boronolide became of interest to us. Hence, a crystal from the original isolation,<sup>1</sup> was subjected to structural investigation by X-ray analysis. The results are presented below.

## RESULTS

Information concerning the structure determination by X-ray techniques is summarized in Table 1. The data collection was carried out using a conventional low temperature device (nitrogen gas stream system). Due to the small anomalous dispersion effects when using

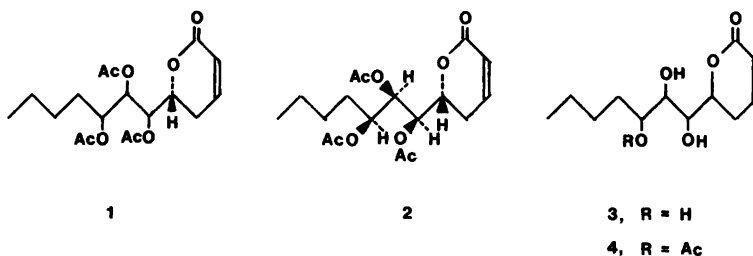


Table 1. Structural data and experimental details on the X-ray diffraction investigation.

Name	Boronolide	Intensity data collection
Formula	$C_{18}H_{26}O_8$	Max. of $\sin \theta/\lambda$ ( $\text{\AA}^{-1}$ )
Formula weight	370.40	Range of $h, k$ and $l$
Space group	$P2_12_12_1$	Standard reffs
Unit cell dimensions ( $\text{\AA}$ )	$\begin{cases} 294 \text{ K} \\ 120 \text{ K} \end{cases}$ $a=6.145(3), b=17.165(3), c=18.712(4)$ $a=6.111(3), b=16.659(4), c=18.560(4)$	Intensity variation
$V$ ( $\text{\AA}^3$ )	$\begin{cases} 294 \text{ K} \\ 120 \text{ K} \end{cases}$ 1974(1) $\text{\AA}^3$ 1889(1) $\text{\AA}^3$	Number of measured reffs
$Z$	4	Number of unique reffs
$D_x$ ( $\text{g cm}^{-3}$ )	$\begin{cases} 294 \text{ K} \\ 120 \text{ K} \end{cases}$ 1.246(1) 1.302(1)	Number of observed reffs
Radiation	MoK $\alpha$	Criterion for observed reffs
$\lambda$ ( $\text{\AA}$ )	0.71069	$R_{\text{int}}$
$\mu$ ( $\text{cm}^{-1}$ )	1.0	Absorption correction
$F(000)$	792	Linear absorption coefficient ( $\text{cm}^{-1}$ )
$T$ (K)	120	Min. and max. transmission
$R$	0.043	Structure determination technique
Crystal colour and shape	Colourless, prismatic	Determination of H-atoms
Crystal size (mm)	$0.04 \times 0.08 \times 0.7$	Structure refinement
Diffractometer	CAD4	Minimization of
Determination of unit cell		Anisotropic model for
Number of reflections used	14	Isotropic model for
$\theta$ -range ( $^\circ$ )	4.9 to 10.5	Parameters fixed for
		Number of parameters
		Weighting scheme
		Final $R$
		Max. final $\Delta/\sigma$
		Max. and min. $\Delta\sigma$ ( $e \text{\AA}^{-3}$ )
		0.60
		0 0 0 to 7 19 22
		2 0 0 and 0 3 4
		Negligible
		2139
		1938
		862
		$\sigma/I < 0.2$
		0.037
		0.996 and 0.998
		Direct methods
		Geometrical
		$\Sigma w(\Delta F)^2$
		O
		C, H
		H (ideal positions)
		145
		$1/(\sigma_F^2 + 0.0005F^2)$
		0.043
		0.052
		0.03
		0.20 and -0.28

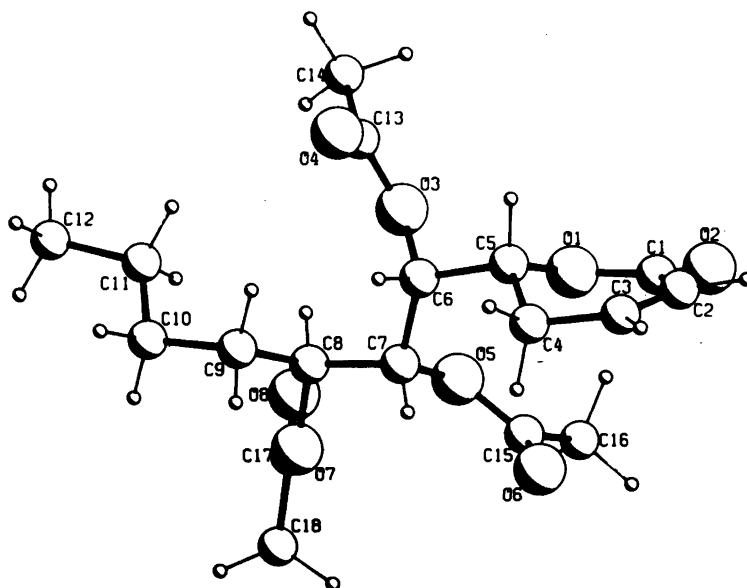


Fig. 1. Atomic labels used and the determined molecular conformation.

Table 2. Fractional atomic coordinates ( $\times 10^4$ ) and thermal parameters ( $\times 10^3 \text{ \AA}^2$ ) of the nonhydrogen atoms. Only the oxygen atoms were allowed to vibrate anisotropically, their equivalent isotropic thermal parameters were estimated as  $\frac{1}{3}$  trace ( $U$ ).

Atom	$x$	$y$	$z$	$U$
O(1)	5913(8)	1874(3)	875(3)	200(15)
O(2)	5379(9)	1242(3)	-151(3)	353(18)
C(1)	6659(13)	1549(5)	261(4)	240(18)
C(2)	9050(13)	1554(5)	150(4)	265(19)
C(3)	10410(14)	1737(5)	679(4)	313(20)
C(4)	9592(12)	1983(5)	1391(4)	245(19)
C(5)	7337(13)	2361(4)	1314(4)	210(18)
C(6)	6247(13)	2526(4)	2028(4)	199(17)
C(7)	5585(13)	1814(4)	2499(4)	192(17)
C(8)	4326(13)	2093(4)	3172(4)	221(17)
C(9)	5612(13)	2671(5)	3645(4)	243(18)
C(10)	4261(13)	3016(4)	4272(4)	259(19)
C(11)	2283(14)	3504(5)	4020(4)	297(20)
C(12)	1345(15)	4006(5)	4609(5)	442(26)
O(3)	4283(8)	2994(3)	1896(3)	222(15)
O(4)	6208(9)	4121(3)	2080(3)	354(19)
C(13)	4486(14)	3800(5)	1939(4)	262(18)
C(14)	2362(13)	4205(5)	1807(5)	348(21)
O(5)	4081(8)	1283(3)	2135(3)	210(15)
O(6)	6791(8)	415(3)	1874(3)	276(17)
C(15)	4896(13)	598(5)	1855(5)	250(19)
C(16)	3174(13)	134(5)	1468(5)	290(19)
O(7)	3915(8)	1381(3)	3591(3)	233(16)
O(8)	283(9)	1503(4)	3401(3)	424(20)
C(17)	1789(14)	1149(5)	3670(4)	266(20)
C(18)	1669(14)	410(5)	4112(4)	338(21)

Table 3. Bond distances (Å) and bond angles (°) between the nonhydrogen atoms.

O(1)–C(1)	1.342(8)	O(1)–C(5)	1.442(8)
O(2)–C(1)	1.208(8)	C(1)–C(2)	1.476(10)
C(2)–C(3)	1.322(10)	C(3)–C(4)	1.471(10)
C(4)–C(5)	1.522(10)	C(5)–C(6)	1.508(9)
C(6)–C(7)	1.528(8)	C(6)–O(3)	1.452(8)
C(7)–C(8)	1.539(10)	C(7)–O(5)	1.443(8)
C(8)–C(9)	1.522(9)	C(8)–O(7)	1.440(8)
C(9)–C(10)	1.538(10)	C(10)–C(11)	1.530(10)
C(11)–C(12)	1.491(10)	O(3)–C(13)	1.351(8)
O(4)–C(13)	1.209(9)	C(13)–C(14)	1.483(10)
O(5)–C(15)	1.349(8)	O(6)–C(15)	1.198(8)
C(15)–C(16)	1.490(10)	O(7)–C(17)	1.363(9)
O(8)–C(17)	1.202(8)	C(17)–C(18)	1.481(10)
O(1)–C(1)–O(2)	119.3(7)	O(1)–C(1)–C(2)	116.9(7)
O(1)–C(5)–O(4)	111.5(5)	O(1)–C(5)–C(6)	109.4(6)
O(2)–C(1)–C(2)	123.7(7)	C(1)–O(1)–C(5)	120.1(6)
C(1)–C(2)–C(3)	121.3(7)	C(2)–C(3)–C(4)	121.2(7)
C(3)–C(4)–C(5)	109.8(6)	C(4)–C(5)–C(6)	113.1(6)
C(5)–C(6)–C(7)	118.6(5)	C(5)–C(6)–O(3)	108.3(5)
C(6)–C(7)–C(8)	111.2(5)	C(6)–C(7)–O(5)	112.1(5)
C(6)–O(3)–C(13)	116.6(6)	C(7)–C(6)–O(3)	107.1(5)
C(7)–C(8)–C(9)	113.7(6)	C(7)–C(8)–O(7)	106.1(5)
C(7)–O(5)–C(15)	117.6(5)	C(8)–C(7)–O(5)	104.3(5)
C(8)–C(9)–C(10)	113.3(6)	C(8)–O(7)–C(17)	117.2(6)
C(9)–C(8)–O(7)	107.4(5)	C(9)–C(10)–C(11)	113.0(6)
C(10)–C(11)–C(12)	112.2(6)	O(3)–C(13)–O(4)	122.2(7)
O(3)–C(13)–C(14)	111.2(7)	O(4)–C(13)–C(14)	126.6(6)
O(5)–C(15)–O(6)	124.1(7)	O(5)–C(15)–C(16)	111.3(6)
O(6)–C(15)–C(16)	124.4(7)	O(7)–C(17)–O(8)	123.1(7)
O(7)–C(17)–C(18)	110.0(7)	O(8)–C(17)–C(18)	126.9(7)

MoK $\alpha$  radiation, attempts to determine the absolute configuration of the structure did not yield statistically significant results. The structural results are presented in Tables 2 and 3.\* The atomic labels used in the structural study and the resulting molecular conformation are shown in Fig. 1.

As the boronolide molecules are devoid of conventional hydrogen bond donors no hydrogen bonds are observed in the crystal structure. Short intermolecular contacts, in the range 3.2–3.3 Å, occur between the carbonyl oxygens and the methyl groups. The H $\cdots$ O distances in these contacts all exceed 2.5 Å indicating normal van der Waals contacts.

The three acetoxy groups of the boronolide molecule are all planar, with root mean square deviations (rmsd's) from least squares (LS) planes through the group ranging from 0.003 to 0.014 Å. In the heptyl chain C(6) to C(12), four of the atoms, C(7) to C(10) and the oxygen O(5), form a planar zig-zag chain with an rmsd of 0.034 Å from an LS plane. The pyran ring (O(1), C(1) to C(5)) takes up a half boat conformation with the C(5) atom as the atom deviating by 0.576 Å from an LS plane through O(1), C(1) to C(4).

\* A list of structure factors, anisotropic thermal parameters, and hydrogen atomic coordinates is available from one of the authors (R.N.) on request.

## DISCUSSION

Accepting the (*R*)-configuration at C-6, derived from chiroptical analyses,<sup>1</sup> the present study unequivocally establishes the structure of boronolide as 6*R*-(1*R*,2*R*,3*S*)-5,6-dihydro-6-[1,2,3-tris(acetyloxy)-heptyl]-2*H*-pyran-2-one, 2. Two structurally related compounds, "deacetylboronolide" 3<sup>2</sup> and "1',2'-dideacetylboronolide" 4,<sup>3</sup> of unspecified stereochemistry, have recently been described, along with other C<sub>12</sub>-lactones, as constituents of *Iboza riparia* (Hochst) N.E.Br., another species of the family Labiatae. Curiously, 3 was reported as devoid of measurable optical activity;<sup>2</sup> no rotation value was quoted for 4.<sup>3</sup>

The acquired knowledge of the stereochemistry of boronolide is currently being exploited in one of the authors' (A.K.) laboratory.

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